

# Gastrointestinal Quality of Life in Gastroesophageal Reflux Disease – a systematic review

Running title: GERD-GIQLI review

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**Abstract:**

**Background:** The Gastrointestinal Quality of Life Index (GIQLI) is a well established instrument for the assessment of Quality of Life (QOL) in gastrointestinal(GI)-diseases. The purpose of this literature review was to investigate QOL by means of GIQLI in patients with Gastroesophageal Reflux Disease (GERD) prior to any interventional therapy. There are several reports on GIQLI-data, however comparisons from different countries and/or different GERD-cohorts assessing the same disease have to date not been conducted.

**Methods:** The GIQL-Index uses 36 items around 5 dimensions (gastrointestinal symptoms (19 items), emotional dimension (5 items), physical dimension (7 items), social dimension (4 items) and therapeutic influences (1 item). A literature search was conducted on the application of GIQLI in GERD-patients prior to interventional therapy using reports in pubmed. Data on the mean GIQLI as well as index-data for the 5 dimensions as originally validated were extracted from the published patient-cohorts. A comparison with the normal healthy control group from the original publication of the GIQLI-validation conducted by Eypasch was performed. Data are presented descriptively as GIQL-Index-points as well as a reduction from 100 % maximum possible index-points (max 144 index-points = highest quality of life).

**Results:** In total, 77 abstracts from studies using the GIQLI on patients with GERD were identified. After screening for content, 21 publications were considered for further analysis. Ten studies in GERD-patients comprized complete calculations of all dimensions and were included in the analysis. Data from 1682 study-patients were evaluated with sample sizes ranging from 33 to 568 patients (median age of 789 female and 858 males: 51,8years). The median overall GIQLI for the patient group was 91,7 (range 86-102,4) corresponding to 63,68 % of the maximum GIQLI. The dimensions with the largest deviation from the respective maximum score were the physical dimension (55% of maximum) followed by the emotional dimension (60% of maximum). In summary, the GIQLI-level in GERD-cohorts was reduced to 55-75 % of the maximum possible index.

**Conclusions:** Severe GERD causes substantial reductions in the patient`s quality of life. The level of GIQLI can vary between different studied GERD-cohorts from

different departments and countries. GIQLI can be used as an established tool to assess the patient's condition in various dimensions.

## **Introduction**

Gastroesophageal Reflux Disease (GERD) has a multifactorial pathophysiologic background [1,2]. Main cause is a malfunction of the antireflux barrier at the Esophago-Gastric Junction (EGJ). The typical symptoms are heartburn and regurgitation [3]. The majority of patients can best be treated with medical therapy such as Protonpump Inhibitors (PPI) [4,5]. In patients suffering from GERD, Quality of Life (QOL) can be substantially reduced by the disease [4,5,6,7]. To date, several validated instruments for the measurement of QOL are available and disease specific instruments have been developed e.g. to assess QOL for malignomas or benign disorders, pre- and postoperative assessment, or for certain organ-systems such as upper GI-tract disease, hepato-biliary and colorectal disorders as well as other diseases [6-15]. QOL is an important factor when evaluating the individual patient's condition, including the patient's psychological and physical well-being during the course of disease, as well as before, during and after treatment [8,9,11,12].

The Gastrointestinal Quality of Life Index (GIQLI) is a well established instrument for the assessment of QOL in gastrointestinal(GI)-diseases and was established, validated and published in German and English 25 years ago [7,8,9]. To date, this instrument has been validated for several other languages, which is an advantage because it makes research on QOL between different countries and cultures comparable, despite culture specific aspects in respective countries [8,9,16-21].

GIQLI-assessment has been broadly used in the surgical literature to determine and compare pre- and postoperative status of the patient's QOL [7, 9,11-14,22,23]. One further advantage of the GIQLI is that it is easy to answer and no supervision of the patients while filling in the forms is required. Besides a global mean, the GIQLI provides 5 different dimensions (gastrointestinal symptoms, the emotional, physical and social factors and a therapeutic component), allowing for a more detailed analysis of the patient's QOL [7-9,12]. The GIQLI is thus also suitable to monitor the patient's social support and network throughout the course of the disease and its treatment.

Another important methodological aspect and advantage could be the availability of data from a population of volunteer participants who identified themselves as healthy (further identified as normal population). It is therefore possible to compare the QOL- status from a normal population to a defined patient group. Several publications are available which provide data from normal control cohorts [8,9,12,22,23]. The GIQLI has been applied in clinical practice and research , providing an effective tool for comparing the patient`s health status and well-being before and after surgical therapy [7-9,11-14]. However, GIQLI-data from different countries and/or different GERD-cohorts assessing the same disease have to date not been conducted.

In order to investigate the level of QOL in this primary disease, the purpose of this study was an analysis of available data regarding GIQLI in patients with GERD assessed prior to any interventional therapy. Thus, a systematic literature search was conducted with the aim to identify publications reporting GIQLI-data in primary GERD. We were interested in the analysis of GERD-cohorts from different institutions and countries with respect to disease severity and other possible factors influencing QOL assessed with the GIQLI In addition, data from clinical cohorts were compared to GIQLI-data from a normal population, reported in literature [9,12].

## **Methods:**

This analysis was part of a larger project, investigating the published data on the application of GIQLI between 1995 and 2021 in several gastrointestinal diseases. In order to evaluate THE QOL-status of GERD-patients, the focus of this particular review was the assessment of GIQLI in this patient group prior to any intervention.

A literature search was performed for reports on the application of GIQLI in pubmed, using the search terms „GIQLI and GERD“ and „GIQLI and gastroesophageal reflux disease“. Primary inclusion criteria were reports on GIQLI-measurements in patients with GERD prior to any invasive therapy. It must be emphasized that we strictly followed the original methodology of the GIQLI-analysis as published and validated [8,9]. QOL was assessed by the GIQL-Index using 36 items around 5 dimensions (gastrointestinal symptoms (19 items), emotional dimension (5 items), physical dimension (7 items), social dimension (4 items) and therapeutic influences (1 item)

[8,9]. The maximum possible values for GIQLI indicating a high QOL, were 76 index-points for gastrointestinal symptoms, 20 points for the emotional dimension, 28 points for the physical dimension, 16 points for the social dimension and 4 points for the influence of therapeutic actions, thus in total maximum 144 index-points (Table 1). The selected articles were checked for the correct application of the GIQLI and its dimensions. Subgroup-1 included all publications which provided the correct analysis and presentation of GIQLI and its 5 dimensions. In subgroup-2, publications were summarized, which provided at least the total sum of GIQLI-points, but were lacking the results of the 5 dimensions.

The selection process followed the PRISMA guidelines as shown in Figure 1 and Table 1-supplement [24]. The abstracts were filtered for presenting data on primary GERD-QOL, double publications of cohorts, inadequate use of the validated methodology of the GIQLI, or any other deviation from the correct use and application of GIQLI. Published studies with a rather low number of participants <30 were excluded, because these were judged as not representative and often their evaluation did not follow the strict assessment rules of GIQLI. The extracted data were grouped according to the GIQLI-dimensions as validated in the original publications. A main focus was the total number of GIQLI-points in the cohort as well as the index-points of the 5 different dimensions.

In addition to the GIQLI-data, available data on patients characteristics such as age, sex, parameters of the severity of the disease (incidence of esophagitis, level of esophageal acid exposure) were documented.

In order to facilitate comparison of the level of GIQLI-points between different study-cohorts, absolute GIQLI-points as well as the percentage of these index-points of the maximally possible GIQLI-points were determined for each dimension.

For the comparison or confrontation of our results with a normal population control group, we relied on the original publication of Eypasch [8,9,12]. The percentage of the GIQLI-points of the results from the normal population and the GERD-cohorts was then compared with regard to the maximum GIQLI-level as well as for each dimension. These results are presented descriptively.

## Results:

Control data from normal population:

The total GIQLI for the 168 normal participants (122,6 points from a maximum of 144 index-points) was obtained from Eypasch [9,12](Table 1). The results for the different dimensions were: gastrointestinal symptoms(GIsym) 62; emotional dimension(emot) 18,5; physical dimension(phys) 23; social dimension(soc) 14,8; therapeutic influence(ther) 3,8. As can be seen, also a normal supposedly „healthy“ population is not likely to achieve total GIQLI-points of 100% (maximum:144). Thus, the data from Eypasch [8,9,12] from a normal population show a deviation of 85-95% from the maximally possible points.

Literature review for publications on GLQLI in patients with GERD:

In total, 77 abstracts were identified with studies using the GIQLI on patients with GERD. After the PRISMA-process, 21 publications were considered for further analysis (Figure 1)[7,12,25-42]. Others were excluded for double publication, inadequate or non-complete evaluation of the GIQLI according to the original methodology as published and validated [8,9,12]. In addition, many studies focused only on postoperative results of antireflux surgery and did not include any preoperative data regarding the disease.

A total of 21 studies was selected for analysis containing at least an overall value of GIQLI-points in patients with GERD prior to any interventional therapy. From the 21 studies selected, a subgroup-1 of 10 studies included a complete calculation of an overall GIQLI-value as well as adequate values for all dimensions, while subgroup-2 (n=11) consisted of studies with a correct GIQLI-analysis, but lacking a detailed dimension-calculation. Table 2 demonstrates the results of subgroup-1 with all dimensions and the accompanying patient`s characteristics..

In subgroup-1 (n=10), data from 1682 study-patients in GERD-populations were evaluated, originating from cohorts with sample sizes from 33 to 568 patients. All

investigated and published cohorts in subgroup-1 originated from surgical series. The median age of 789 female and 858 males was 51,8 years.

The median overall GIQLI was 91,7 (range 86-102,4) corresponding to 63,7 % of the maximum possible index-value. The physical dimension was most affected (55% of maximum) followed by the emotional dimension (60% of maximum). Table 2 demonstrates the reduction of GIQLI compared to the maximal possible GIQLI-value for GERD patients. The GIQLI-level in GERD-cohorts is reduced to levels between 55-75 % of the maximum, which corresponds to a substantial QL-reduction in all dimensions, especially in the physical and emotional dimensions. When this reduction is compared to control group-data of a normal population [2], the reduction of the latter from maximum index-values ranges is around 10-15%.

Further analysis of subgroup-1 between age and total GIQLI-points across studies was not significant ( $r=0,014$ ). Furthermore, there was no significant correlation between the total GIQLI-points and other clinical parameters such as the presence of esophagitis and the level of pathologic acid exposure as measured by 24h-pH-monitoring in those studies that provided such information ( $r<0,5$ ). Figure 2 demonstrates the distribution of GIQLI-levels in subgroup-1.

In subgroup-2, 11 studies were analysed, presenting total GIQLI-points of the cohorts *without* detailed analysis of dimensions (Table 3). There were another 1742 study-patients in GERD-populations investigated; 719 females and 875 males had a median age of 50,1 years. The median overall GIQLI in these cohorts was 92,2 (range 78-129), which represents a GIQLI-reduction to 64 % of maximum index-points (Table 3). It must be noted that there was one cohort within subgroup-2 representing a real outlier with a median GIQLI of 129 in a publication from a medically treated GERD-cohort. Despite this outlier, the results of subgroup-2 suggest a similar GIQLI-level as in subgroup-1.

## **Discussion:**

The analysis of publications on GERD-studies with measures of GIQLI shows substantial differences in the level of QOL-reductions among the various publications and cohorts, reaching from 78 to 129 GIQLI-points [7,12,25-42]. There are also

differences between GERD-cohorts from different surgical studies. The largest difference can be noticed between the bulk of surgical cohorts and one study from gastroenterologists, following up a large cohort of GERD-patients and stating a remarkable high level of GIQLI in these patients under PPI-therapy [37]. Again, the majority of the selected studies were originating from surgical units usually derived from a preoperative setting [7,12,25-36,38-42]. Therefore, it must be emphasized that most of these GERD-cohorts are patients with a probably more severe disease, often prior to antireflux surgery or at least considering such a therapeutic option.

Therefore, these cohorts are most likely not comparable, since patients in the preoperative situation are usually also under high-dosage PPI-therapy and the insufficient effect of this treatment option with persisting problems is the main reason for considering antireflux surgery for these patients [25,31]. Nonetheless, the inclusion of this study is important because it shows, that patients can achieve a normal GIQLI under PPI-medication [37].

However, it also shows, how affected the QOL can be in patients, where PPI-therapy fails and is insufficient to achieve appropriate symptom relief [25,31]. It is this patient group, which usually presents at surgical units with the question whether a surgical intervention is necessary. Consequently, it is fundamental to carefully evaluate the patient's symptom load, parameters of the severity of disease such as esophageal acid exposure, incompetence of the Esophago-Gastric-Junction and esophageal mucosal damage to get a more complete picture of a given patient [1,2,4,5,43].

In addition, quality of life of a person is determined by many factors or dimensions, which may in some persons correlate with the severity of symptoms, in others it may be multifactorial determined also by social and/or emotional influences as well [1,2,4,5,44-49]. Therefore, the comparison of different studies on GERD-patients performed in different environments (for example different selection of patients for functional, endoscopic or psychologic investigations) with different cohorts, is not only of scientific and academic value. To compare different clinical populations with different GIQLI-points can provide an overview over the total span of symptom-severity for the clinician, providing an additional tool for clinical decision-making [4,5,12,25,31,41,43]. While a normal QOL-level in patients with GERD should encourage the managing therapists to be cautious in favouring a decision for



interventional and surgical therapy, a substantial reduction in quality of life should in any case motivate any physician to further investigate the reasons for such a deleterious QOL.

In patients with GERD-symptoms, symptom-overlap with other functional disorders such as functional heartburn, hypersensitive esophagus, esophageal motility disorders and somatoform disorders may occur [5,31,44-49]. These factors may also severely reduce the patient's quality of life, however, a surgical intervention will most likely not lead to symptom improvement in such a complex clinical picture [31,40]. Thus, further functional and morphologic investigations are needed to identify the underlying pathology leading to the increased symptom load [1,2,4,5,41,43].

The application of a validated instrument to assess QOL in patients with a given disease allows for a comparison of this patient's QOL with a level of normal controls in order to make a judgement about the amount of QOL-reduction this patient may suffer. Alternative instruments to assess QOL are available in literature [6,10,13,15,50-52]. The often applied GERD-Health-related-Quality-of-Life score (GERD-HRQL) represents basically a symptom-presence and symptom-intensity-score which consists of an assessment-scale from 0-50, 50 being the worst possible measure [6,50-52]. The GERD-HRQL has been promoted by several authors and [6,50-52]. We have initially chosen the GIQLI as QOL-tool because of its applicability in all GI-diseases. These complex clinical situations underline the necessity to investigate QOL in patients using a validated and widely used instrument such as the GIQLI. Such an approach allows for the comparison of own data with other reports and especially with control data in literature. Systematic investigation and evaluation of QOL with a standardized instrument will improve daily clinical evaluations and judgement of patients.

### **Conclusions:**

Severe GERD causes substantial reductions in the patient's quality of life which can be well documented by the GIQLI. The latter has been applied over 25 years in clinical medicine and thus, has been established especially among surgeons as a dependable tool to objectively assess the patient's condition in various dimensions.

This does not only allow for use of GIQLI to compare different patient's cohorts regarding their status, it furthermore provides a means to improve clinical practice.

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**Statements of ethics:**

An ethics statement and written informed consent are not applicable because this study is based exclusively on published literature.

**Conflict of Interest statement:**

None of the authors have any conflict of interest nor any financial disclosures regarding the theme and the data of this manuscript. Karl-Hermann Fuchs, Frauke Musial, Ernst Eypasch and Alexander Meining declare that they have no conflict of interest.

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**Author contributions:**

Karl-Hermann Fuchs, Frauke Musial, Ernst Eypasch and Alexander Meining had substantial contributions in the study concept and design. Karl-Hermann Fuchs, Frauke Musial, Ernst Eypasch and Alexander Meining had substantial contributions in the analysis and interpretation of the data in the literature review and selection during the PRISMA process. Karl-Hermann Fuchs, Frauke Musial, Ernst Eypasch and Alexander Meining had substantial contribution in the drafting of the manuscript, revising of the manuscript and the final approval of the manuscript to be published.

Karl-Hermann Fuchs, Frauke Musial, Ernst Eypasch and Alexander Meining agree to be accountable for all aspects of the work and ensuring its accuracy and its integrity.

**Data availability statement:**

All data generated or analysed during this study are included in this article. The data are published in literature as shown in the reference list. Further inquiries can be directed to the corresponding author.

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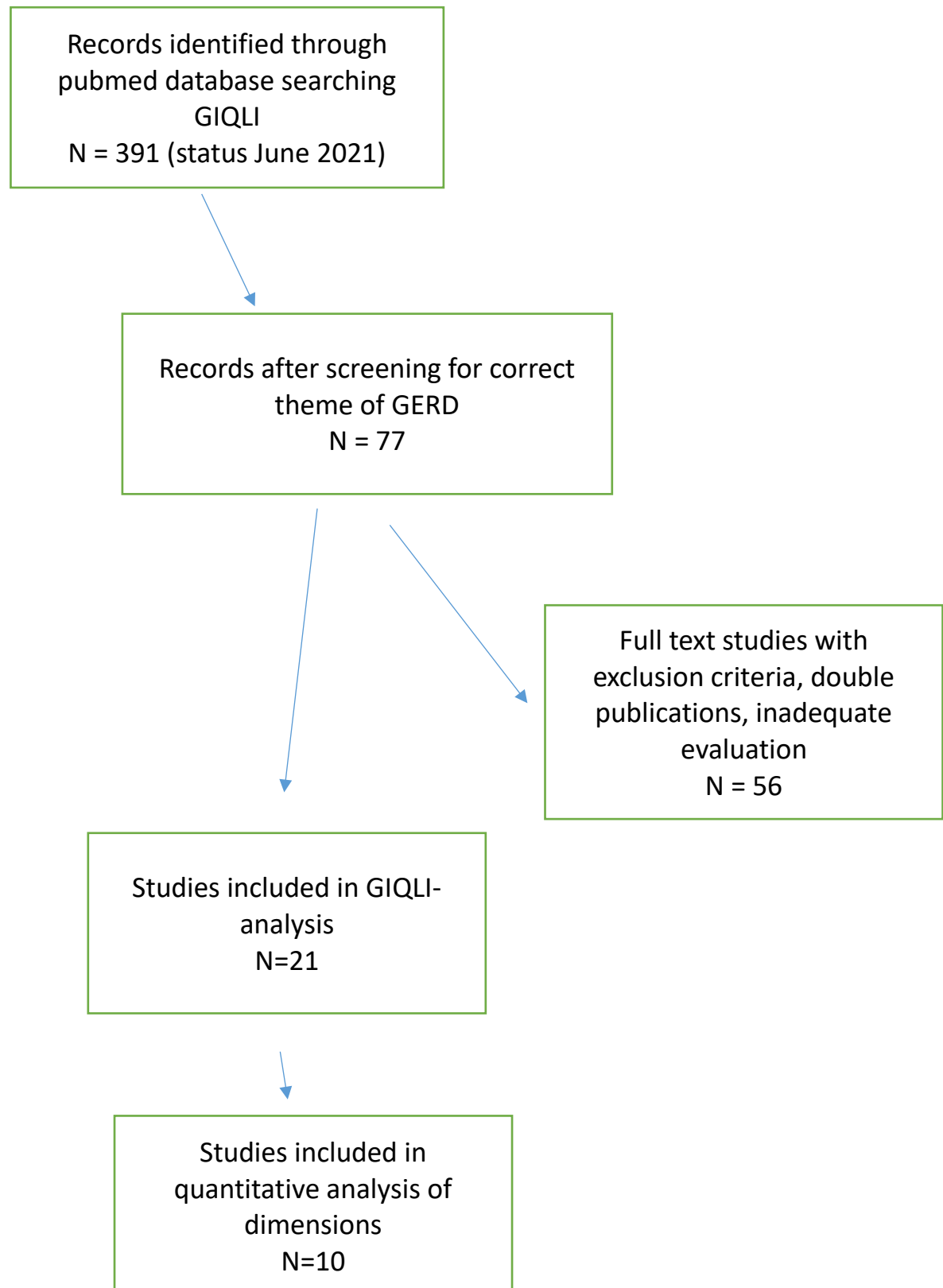


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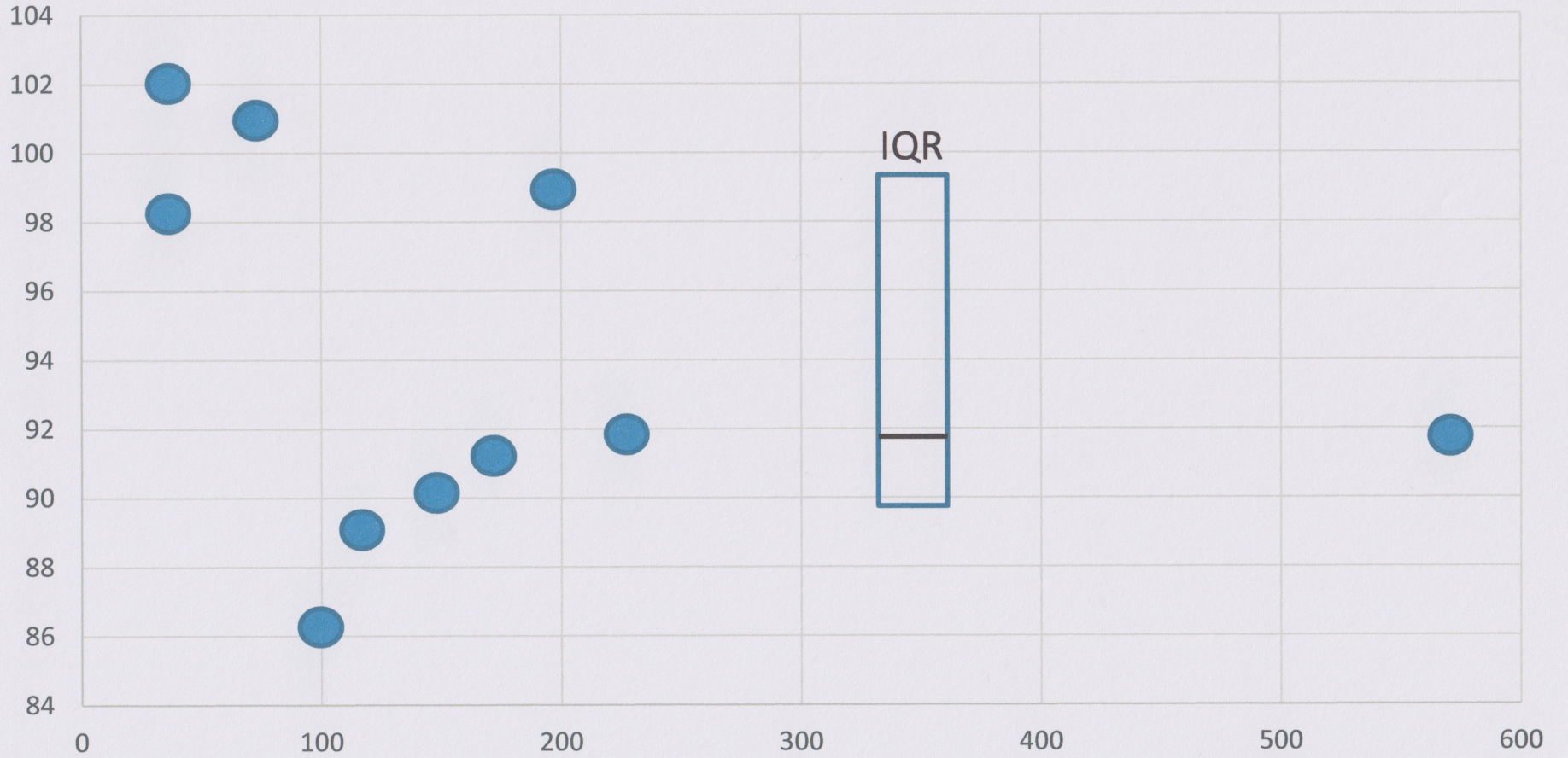
## Legend of Figures:

Figure 1: PRISMA-overview on the selection of publications and the final sample of adequate studies for analysis of GERD and GIQLI

Figure 2: Plot-graph of the GIQLI-level regarding the cohort-size of the different published studies in subgroup-1



# GIQLI



number of patients

Table 1: GIQLI by Eypasch (1995) in healthy volunteers of validation population from [8,9,12] and display of percentage of „normal“ GIQLI from maximum index-points

	n	sex: female/ male	mean age	GI- symp	emot	phys	soc	ther	GIQLI mean
volunteers	168	76/92	42	62	18,5	23,5	14,8	3,8	122,6
Maximum index-points of GIQLI				76	20	28	16	4	144
<i>Percentage of maximum (%)</i>				<i>81</i>	<i>92</i>	<i>84</i>	<i>91</i>	<i>95</i>	<i>85</i>

Table 2: Overview on results in literature regarding GIQLI and all dimensions in surgical patient-cohorts with GERD

Author Department year	n	gender: female/ male	mean age	itis	Acid expo	GI- symp	emot	phys	soc	ther	GIQLI mean
Kamolz; surg 2000 [7]	175	78/97	52,1	-	Mean 63,7	47,9	12,3	15,2	12,2	2,8	90,4
Granderath; Surg, 2002,[12]	150	48/102	51,8	-	62,9	45,9	12,9	15,4	12,9	3	90,1
Dallemagne; Surg; 2006 [25]	100	38/62	52	85%	Path 88%	48	10	14	11	3	86
DiazdeLiano; Surg; 2006 [26]	73	25/48	40	-	-	53	14	20	11	3	101
Wang <70y; Surg; 2008 [27]	198	71/127	46,6	-	-	53,8	11,6	18,2	12,4	2,4	98,8
Wang >70y; Surg; 2008 [27]	33	21/13	73	-	-	52,3	13,5	19,3	12,3	2,6	102,4
Fein; surg 2008 [28]	120	41/79	49	60%	Mean 45,8	49	11	14	12	3	89
Borie; surg 2010 [29]	35		49,5	52%	28%	55	13	16	11,7	2,5	98
Fuchs; surg 2011 [30]	230		48	62%	Mean 48,7	50	12	15	12	3	92
Fuchs; surg 2021 [31]	568	339/229	52,9	66%	76,4%	49,6	11,5	15,4	11,9	2,9	91,4
ranges						45,9- 55	10- 13,5	14- 20	11- 12,9	2,4- 3	86- 102,4
median						50	12	15,3	12	3	91,7
% of maximum						66	60	55	75	75	64

Table 3: Overview on results in literature regarding GIQLI *lacking dimensions* in patient-cohorts with GERD

First author	year	n	gender: female/ male	mean age	GIQLI	Std Dev
Heikkinen; surg [32]	2000	42	16/25	48	78	
Slim; surg [33]	2000	50	20/30	49,9	95	
Zügel; surg [34]	2002	122	41/81	46,6	86,6	10,2
Ciovica; surg+medical [35]	2006	579	231/348	52	95	
Yano; surg [36]	2009	54		51,5	84	19,5
Lippmann, medical [37]	2009	530	270/259	50,3	129	
Zhu; surg [38]	2011	30	20/10	71	85,7	12,1
Luketina; surg [39]	2015	40	17/23	49,9	93,7	18,1
Weitzendorfer; Surg [40]	2018	40	22/18	49,8	92,5	18,5
Fuchs HF; surg [41]	2019	166	82/81	58	99	
Khoma,; surg [42]	2020	89		84	91,8	19,4
ranges					78-129	
median					92,2	
% of GIQLI maximum					64%	